REMARKS

I. Status of the Claims

Without prejudice or disclaimer, claims 1-17 have been cancelled. New claims 18-34, which correspond to claims 18-34 in parent application no. 09/643,197, have been added. Support can be found throughout the specification and claims as originally filed. No new matter has been added.

II. Rejection under 35 U.S.C. § 112, First Paragraph

Claims 18-30 and 32-34 in parent application no. 09/643,197 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter allegedly not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. (Application no. 09/643,197, Office Action of September 3, 2003, pg. 2.) The Examiner more specifically contended that:

> (1) "It is asserted in the specification that the claimed compounds are effective to inhibit growth of bacteria. However, there is no evidence that this is the case." (*Id*, pg. 2.)
>
> (2) "With regard to the 'pharmaceutical composition,' this term carries with it the implied assertion of therapeutic efficacy. As it happens, *in vitro* efficacy is not necessarily predictive of *in vivo* efficacy." (*Id.*, pg. 4.)

Applicants respectfully traverse the rejection for the reasons of record in parent application no. 09/643,197, and as discussed further below.

1. Evidence of *In Vitro* and *In Vivo* Antibacterial Efficacy

In addition to the data and information provided in the present specification (see, e.g., pg. 7, line 21 to page 8, line 10; pg. 33, ln. 1-4; pg. 33, ln. 5-11), and as further discussed on the record in prior application no. 09/643,197, Applicants now provide the

following additional data and information further demonstrating that the claimed invention is fully enabled.

As shown by the results presented in the accompanying Declaration Under 37 C.F.R. § 1.132 of Dr. Nadine BERTHAUD, streptogramin compounds according to general formula (I) of the presently claimed invention (see, e.g., claim 18) have proven active *in vitro* against *Staphylococcus aureus* 209P at concentrations of as low as 1 µg/ml, and in combination with pristinamycin IIB ("PIIB"), have proven active at concentrations of 0.25 to 10 µg/ml. Additionally, compounds according to general formula (I) in combination with PIIB have proven effective *in vitro* against *S. aureus Schiclia* at concentrations ranging from 0.5 to 4 µg/ml. In the combination treatments, the results show that, in nearly every instance, the activity of the combination is enhanced over either the streptogramin formula (I) compound or PIIB, when tested individually. For instance, against *S.aureus* 209P, the Minimum Inhibitory Concentration ("MIC") activities of compound 1 and PIIB, tested individually, were 8 and 4 µg/ml, respectively, while in combination the MIC activity was 0.5 µg/ml. Further, against *S.aureus Schiclia*, the MIC activities of compound 1 and PIIB, tested individually, were >128 and 4 µg/ml, respectively, while in combination the MIC activity was 2 µg/ml.

In vivo, streptogramin compounds according to general formula (I) have proven effective, as measured by their curative dose 50 ("DC_{50}"), against *Staphylococcus aureus* IP 8203 test infections in mice in subcutaneous doses of 25 to 150mg/kg combined with dalfopristin, and with orally administered doses of 15 to 150mg/kg

combined with pristinamycin IIB.[1] These results can be compared to an activity of > 300 mg/kg for dalfopristin and pristinamycin IIB, when each is tested individually in analogous *in vivo* tests. Thus, the combination treatments were more potent in their DC_{50} than either dalfopristin and pristinamycin IIB taken individually.

2. Conclusion with respect to rejection under 35 U.S.C. § 112, first paragraph.

As discussed above, there is a significant amount of evidence of record that the claimed compounds have antibacterial activity both *in vitro* and *in vivo*. Therefore, since the rejection was premised on the contentions that (1) there is no evidence that the claimed compounds are effective to inhibit growth of bacteria (Application no. 09/643,197, Office Action of September 3, 2003, pg. 2), and (2) "[w]ith regard to the 'pharmaceutical composition,' this term carries with it the implied assertion of therapeutic efficacy [but] *in vitro* efficacy is not necessarily predictive of in vivo efficacy" (*id.*, pg. 4), Applicants respectfully requests reconsideration and withdrawal of the rejection.

III. Rejection under 35 U.S.C. § 112, Second Paragraph

Claim 33 in parent application no. 09/643,197 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claim 33 was rejected, apparently for its reference to Streptogramin A derivatives by their common name, such as pristinamycin II_B, and not their chemical name or structure. (Application no. 09/643,197, Office Action of September 3, 2003, pg. 9 ("Claim 33 makes reference to various group A streptogramin derivatives such as pristinamycin II_B. However, this renders the claim

[1] For compound 23, the *in vivo* activity (DC_{50}) with dalforprisin was only determined to be something greater than 150 mg/kg. Higher doses were not tested to more precisely determine the DC_{50}.

indefinite. It is suggested that a chemical name or structure be provided for each of the listed compounds.") Applicants respectfully traverse the rejection.

There is nothing improper in using terms, such as common names for compounds, if they are well known and understood in the art. *E.g., In re Miller*, 164 USPQ 597, 599 (CCPA 1971). In the present case, the relevant common names, such as pristinamycin II_B, which are used, are well known in the art. *See, e.g.,* J.C. Barrière et al., Current Pharmaceutical Design, 4, 155-180 (1998) (referring at pg. 156 to, *inter alia*, pristinamycin II_A, IIB, IIC, IID, IIE, IIF, and IIG) (copy previously provided). Likewise, Applicants direct the Examiner's attention to V. Blanc et al., J. Bacteriology 177 (18), 5206-5214 (1995) (courtesy copy enclosed), which includes discussion of streptogramin derivatives including pristinamycin IIA and IIB, and to C. Chant et al., The Annals of Pharmacotherapy, 29, 1022-1027 (1995) (courtesy copy enclosed), which identifies pristinamycin IIA as a Group A stretogramin derivative.

As further evidence that one skilled in the art would understand reference to streptogramin compounds based on their common names, enclosed herewith is the Declaration Under 37 C.F.R. § 1.132 of Dr. BERTHAUD, which states that in the declarant's experience "streptogramin A compounds are often identified by common names," and in the declarant's opinion "one skilled in the art would understand the reference to a streptogramin A compound based on its common name." (Declaration of BERTHAUD, at 8.)

Should the Examiner maintain the present rejection, Applicants expressly request that the Examiner provide evidence on the record, either in the form of a citation to relevant art or in the form an affidavit under 37 CFR § 104(d)(2), to support the

Examiner's position. Absent any such evidence, Applicants respectfully submit that it would be improper for the rejection to be maintained, especially in view of Applicants' above cited evidence.

Reconsideration and withdrawal of the rejection are, therefore, respectfully requested.

IV. Conclusion

Applicants respectfully request the timely allowance of the pending claims.

Please grant any extensions of time required to enter this paper and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: August 10, 2004

By: _____
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Attachments:

Substitute Abstract
V. Blanc et al., J. Bacteriology 177 (18), 5206-5214 (1995)
C. Chant et al., The Annals of Pharmacotherapy, 29, 1022-1027 (1995)